Food and Drug Administration
Center for Drug Evaluation and Research

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SUMMARY MINUTES
ARTHRITIS ADVISORY COMMITTEE

March 24, 1998
Gaithersburg Hilton
620 Perry Parkway, Gaithersburg, MD

Members Present
Michelle Petri M.D., M.P.H.,Chair
Steven B. Abramson, M.D.
David Yocum, M.D.
Leona Malone, MSW
Frank Pucino, Jr., Pharm.D.
E. Nigel Harris, M.D.
Matthew Liang, M.D., M.P.H.
Lee Simon, M.D.

FDA Participants
Michael Weintraub, M.D.
Kent R. Johnson, M.D.
James P. Witter, M.D.
John Hyde, M.D., Ph.D.

Consultants
Felix Fernandez-Madrid, M.D., Ph.D.
Ildy Katona, M.D.
Larry Moreland, M.D.
Leigh Callahan, Ph.D.
Kevin McConnell, M.D.
Kenneth Brandt, M.D.
Loren Laine, M.D.

Guest Experts

Members Absent
Barbara Tilley, Ph.D.
Daniel Lovell, M.D., M.P.H.
Harvinder Luthra, M.D.

Executive Secretary
Kathleen R. Reedy

These summary minutes for the March 24, 1998 meeting of the Arthritis Advisory Committee were approved on 8/26/99.

I certify that I attended the March 24, 1998 meeting of the Arthritis Advisory Committee and that these minutes accurately reflect what transpired.

Kathleen R. Reedy
Kathleen R. Reedy,
Executive Secretary

Michelle Petri
Michelle A. Petri, M.D., M.P.H.
Chairperson

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The Arthritis Advisory Committee met on March 24, 1998 at the Gaithersburg Hilton, 620 Perry Parkway, Gaithersburg, MD to discuss the safety issues; gastro-intestinal tolerability, renal, bone and reproductive toxicity related to NSAID COX-2 and other agents. The committee had been provided a briefing document from the agency as background for the discussion of issues approximately 15 days before the meeting. There were approximately 200 people in attendance.

The meeting was called to order at 8:00 by Michelle Petri, M.D., Chair of the Arthritis Advisory Committee. The Meeting Statement was read by Kathleen Reedy, Executive Secretary of the Arthritis Advisory Committee. The Committee members and consultants introduced themselves. A welcome and introduction to the topic by Michael Weintraub, M.D., Acting Director, Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products began the discussion.

There were two speakers at the Open Public Hearing. Steven Geis, M.D., Executive Director, Clinical Research at Searle and Robert Palmer, M.D., Director of Rheumatology at SmithKline Beecham Pharmaceuticals.

Loren Laine, M.D., a Gastroenterologist and member of the GastroIntestinal Drugs Advisory Committee presented an overview of the gastrointestinal effects of NSAIDs followed by questions and discussion by the Committee. Kevin R. McConnell, M.D., a Nephrologist and Consultant to the Arthritis Advisory Committee gave a presentation on the renal effects of NSAIDs followed by questions and discussion.

The committee's general discussion was conducted around the following topics.

Studies
Endpoints
Labeling
Concomitant conditions/medication
Statistical Analysis

These questions were addressed with discussion by the committee.

I. What constitutes the type of adequate and well controlled studies which will be clinically meaningful?

II. The following questions relate to clinical trial designs attempting to demonstrate clinically meaningful improvement in GI safety:

1. What constitutes the type of adequate and well controlled study(ies) which will support changes to the NSAID GI Warning (e.g. large and simple, endoscopy)?

2. What kinds of endpoints should be considered for improved GI safety?

3. What constitutes an adequate length of study(ies) to support changes to the NSAID GI Warning?

4. In these studies, what dose(s) and type(s) of study comparators should be used, e.g. placebo, other NSAIDs, the "X" dose of the test product, etc. ?

5. What types of patients and medications should be included or excluded for these studies, e.g. OA vs. RA, H.Pylori, concomitant medications, etc.?

6. What statistical analysis should be used for these studies to support changes in the NSAID GI Warning?

III Additionally, we would like to discuss renal, bone, and reproductive toxicity associated with COX-2 and other agents. This discussion would include types of studies, endpoints, dose, duration, comparators, exclusion/inclusion criteria and types of patients to adequately address these concerns.

A verbatim transcript of the meeting is available for more detailed examination of the discussion issues.

The meeting was adjourned at approximately 5:00 pm.